## Remarks

The Office Action mailed December 3, 2002 has been received and reviewed. Claims 22-31 having been cancelled (claims 1-3 and 9-13 previously cancelled), claims 4, 6-8, 14, 16-18, and 32 having been amended, and claims 33-44 having been added, the pending claims are claims 4-8, 14-21, and 32-44. Reconsideration and withdrawal of the rejections are respectfully requested.

The specification has been amended to clarify that the sequence identification numbers refer to the all L-form of the sequence where appropriate.

Claims 4 and 14 have been amended to remove the sequence identification numbers because the sequences claimed are in the all D-form and are not required to have sequence identification numbers per MPEP § 2422.01 and 37 CFR § 1.821(a)(2).

Claims 6-8 and 16-18 have been amended to refer to melanoma cells, which is fully supported by the specification. Claims 16-18 have been amended to incorporate language from the preamble into the body of each claim.

Support for the amendment to claim 32 is in the specification at page 7, line 22.

The new claims are fully supported by the specification and originally filed claims.

No new matter has been added.

## Election/Restrictions

The Examiner withdrew claims 22-31 from consideration as being directed to a non-elected invention. Applicants have cancelled claims 22-31, thereby rendering any objection the Examiner may have to these claims moot.

## The 35 U.S.C. §112, First Paragraph, Rejection

The Examiner rejected claims 6-8 and 16-21 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is rendered moot in view of the amendments to the claims, which have been amended either directly or indirectly to refer to melanoma tumor cells and a polypeptide consisting of the sequence gly-val-lys-gly-asp-lys-gly-asn-pro-gly-trp-pro-gly-ala-pro in the all D-form.

It is respectfully submitted that the specification provides sufficient detail to enable one of skill in the art to carry out the invention commensurate with the scope of the claims. Reconsideration and withdrawal of this rejection is respectfully requested.

**The 35 U.S.C. §112, Second Paragraph, Rejection**

The Examiner rejected claims 16-21 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner objected to the U.S.C. of the term "modulating" and the lack of a statement in the body of the claim that recites back to the preamble. This rejection is traversed.

The claims have been amended to include phrases that relate back to the preambles, which should address both of the Examiner's concerns, particularly in view of the definition in the specification of "modulating" at page 5, lines 11-13, which renders the claims sufficiently clear to one of skill in the art.

**The 35 U.S.C. §102 Rejections**

The Examiner rejected claims 4 and 6-8 under 35 U.S.C. §102(b) as being anticipated by Knutson et al. The Examiner also rejected claim 32 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,013,628-A. These claims have been amended, thereby rendering these rejections moot.

Insofar as the rejection over Knutson et al. applies to the presently pending claims, the

Examiner's attention is directed to the accompanying Declaration of Professor Gregg Fields, which states that the polypeptide referred to in Knutson et al. at the time was not the same as the polypeptide of claim 4. Specifically, the polypeptide of Knutson et al. included a tyrosine not present in the polypeptide of claim 4.

**The 35 U.S.C. §103 Rejection**

The Examiner rejected claims 4-8, 14, 15, and 32 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,013,628-A in view of Dooley et al. (*Science*, *266*:2019-2022, 1994). The Examiner further rejected claims 4-8, 14, 15, and 32 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,082,926-A in view of Dooley et al. (*Science*, *266*:2019-2022, 1994) and U.S. Patent No. 6,274,704-B1.

These rejections are rendered moot in view of the amendments to the claims. In the event that these rejections are maintained, they are respectfully traversed.

There is no teaching or suggestion of the claimed polypeptide (in the all D form) or peptide-conjugates (all D or all L form), or that such polypeptide or peptide-conjugates can be used in the claimed methods dealing with melanoma tumor cells. Assuming that the Examiner is correct in stating that the cited documents provide a motivation, this motivation is at best an invitation to try. There is no expectation of success provided by the cited documents. Thus, Applicants request reconsideration and removal of these rejections.

**Obviousness-Type Double Patenting Rejection**

The Examiner rejected claims 4-8, 14, 15, and 32 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 5,082,926-A in view of Dooley et al. (*Science*, *266*:2019-2022, 1994) and U.S. Patent No. 6,274,704-B1 for the reasons set forth in the 35 U.S.C. §103(a) rejection above.

These rejections are rendered moot in view of the amendments to the claims and further in view of the arguments presented above. In the event that the rejections are maintained, upon

## Summary

It is respectfully submitted that the pending claims 4-8, 14-21, and 32-44 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

CERTIFICATE UNDER 37 C.F.R. 1.8:

CERTIFICATE UNDER 37 CFR §1.8: The undersigned hereby certifies that this paper is being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Assistant Commissioner for Patents, Washington, D.C. 20231, on this 3RD day of April, 2003, at 4:15 pm. (Central Time).

By: _____
Name: KATHLEEN L. FRANKLIN

April 3, 2003
Date

Respectfully submitted for
**FIELDS et al.**

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**APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE**

Serial No.: 09/529,691

Docket No.: 110.00680101

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been shaded.

**In the Specification**

The paragraph beginning at page 5, line 16, has been amended as follows:

Figures 1A and 1B show the relative inhibition of M14#5 human melanoma cell adhesion to 10 µg/mL type IV collagen (TIV), fibronectin (FN), laminin (LM), or bovine serum albumin (BSA) by 100 µg/mL of L-IVH1, D-IVH1, or RI-IVH1 (a polypeptide having the sequence pro-ala-gly-pro-trp-gly-pro-asn-gly-lys-asp-gly-lys-val-gly (all-L-form; SEQ ID NO:3), which is the all-D form synthesized in the reverse order and referred to as "Retro-Inverso"). Cells were preincubated with the peptides for 15 minutes and then added to the wells in the presence of the peptides for a 30-minute incubation period at 37°C. The data represent the means of triplicate points plus or minus the standard errors of the means. Figures 1A and 1B represent different experiments run under the same conditions.

The paragraph beginning at page 5, line 27, has been amended as follows:

Figure 2A and B show the inhibition of M14#5 human melanoma cell invasion through MATRIGEL by 500 µg/mL (A) or 1 mg/mL (B) of L-IVH1, D-IVH1, or RI-IVH1 (a polypeptide having the sequence pro-ala-gly-pro-trp-gly-pro-asn-gly-lys-asp-gly-lys-val-gly (all-L-form; SEQ ID NO:3), which is the all-D form synthesized in the reverse order and referred to as "Retro-Inverso"). Cells were mixed with the peptides and then tested for their ability to invade through MATRIGEL basement membrane (obtained from Collaborative Biomedical Products). The data represents the means of triplicate points plus or minus the standard errors of the means.

In the Claims

For convenience, all pending claims are shown below.

4. (AMENDED) A polypeptide having consisting of the sequence gly-val-lys-gly-asp-lys-gly-asn-pro-gly-trp-pro-gly-ala-pro (SEQ ID NO: 1), which is in the all D-form.

5. The polypeptide of claim 4 further comprising a cytotoxic agent covalently bonded thereto.

6. (AMENDED) The polypeptide of claim 4 which inhibits binding of melanoma tumor cells to type IV collagen.

7. (AMENDED) The polypeptide of claim 4 which inhibits melanoma tumor cell invasion into basement membranes.

8. (AMENDED) The polypeptide of claim 4 which inhibits melanoma tumor cell metastasis.

14. (AMENDED) A peptide-conjugate comprising a polypeptide having the sequence gly-val-lys-gly-asp-lys-gly-asn-pro-gly-trp-pro-gly-ala-pro (SEQ ID NO: 1), which is in the all D-form, wherein the polypeptide is bonded to a non-peptide moiety.

15. The peptide-conjugate of claim 14 further comprising a cytotoxic agent covalently bonded thereto.

16. (AMENDED) A method of inhibiting melanoma tumor cell binding to type IV collagen comprising contacting the melanoma tumor cell with the polypeptide of claim 4 for a peptide-conjugate of claim 14 in amount effective to inhibit melanoma tumor cell binding to type IV

collagen.

17. (AMENDED) A method of inhibiting melanoma tumor cell invasion of a basement membrane comprising modulating the melanoma tumor cell with a the polypeptide of claim 4 or a peptide conjugate of claim 4 in an amount effective to inhibit melanoma tumor cell invasion of a basement membrane.

18. (AMENDED) A method of inhibiting melanoma tumor cell metastasis comprising modulating the melanoma tumor cell with a the polypeptide of claim 4 or a peptide conjugate of claim 4 in an amount effective to inhibit melanoma tumor cell metastasis.

19. The method of claim 16 which is carried out *in vivo*.

20. The method of claim 17 which is carried out *in vivo*.

21. The method of claim 18 which is carried out *in vivo*.

22. CANCEL

23. CANCEL

24. CANCEL

25. CANCEL

26. CANCEL

27. CANCEL

28. CANCEL

29. CANCEL

30. CANCEL

31. CANCEL

32. (AMENDED) A peptide-conjugate comprising a polypeptide having the sequence gly-val-lys-gly-asp-lys-gly-asn-pro-gly-trp-pro-gly-ala-pro [redacted], which is in the all L-form, wherein the polypeptide is bonded to a non-peptide moiety selected from the group consisting of an organic group having a [redacted] alkyl chain, [redacted], a DNA intercalator, a metal chelator, an alkylating agent, and a membrane-disrupting agent.

33. (NEW) A method of inhibiting melanoma tumor cell binding to type IV collagen comprising contacting the melanoma tumor cell with a peptide conjugate of claim 14 in an amount effective to inhibit melanoma tumor cell binding to type IV collagen.

34. (NEW) A method of inhibiting melanoma tumor cell invasion of a basement membrane comprising modulating the melanoma tumor cell with a peptide conjugate of claim 14 in an amount effective to inhibit melanoma tumor cell invasion of a basement membrane.

35. (NEW) A method of inhibiting melanoma tumor cell metastasis comprising modulating the melanoma tumor cell with a peptide conjugate of claim 14 in an amount effective to inhibit

melanoma tumor cell metastasis.

36. (NEW) The method of claim 33 which is carried out *in vivo*.

37. (NEW) The method of claim 34 which is carried out *in vivo*.

38. (NEW) The method of claim 35 which is carried out *in vivo*.

39. (NEW) A method of inhibiting melanoma tumor cell binding to type IV collagen comprising contacting the melanoma tumor cell with a peptide conjugate of claim 32 in an amount effective to inhibit melanoma tumor cell binding to type IV collagen.

40. (NEW) A method of inhibiting melanoma tumor cell invasion of a basement membrane comprising modulating the melanoma tumor cell with a peptide conjugate of claim 32 in an amount effective to inhibit melanoma tumor cell invasion of a basement membrane.

41. (NEW) A method of inhibiting melanoma tumor cell metastasis comprising modulating the melanoma tumor cell with a peptide conjugate of claim 32 in an amount effective to inhibit melanoma tumor cell metastasis.

42. (NEW) The method of claim 39 which is carried out *in vivo*.

43. (NEW) The method of claim 40 which is carried out *in vivo*.

44. (NEW) The method of claim 41 which is carried out *in vivo*.